CLAIMS

1. Composition useful in gene therapy comprising stabilized particles of cationic transfection agent(s)/nucleic acid complexes, characterized in that it incorporates, in addition, at least one nonionic surface-active agent in a sufficient quantity to stabilize the size of the said particles at a size of less than or equal to 160 nm.

2. Composition according to claim 1, characterized in that the cationic transfection agent and the nucleic acid are present therein in a charge ratio of between 1 and 6.

3. Composition according to claim 1 or 2, characterized in that the cationic transfection agent and the nucleic acid are present therein in a charge ratio of less than 4.

4. Composition according to one of the preceding claims, characterized in that the surface-active agent comprises at least one hydrophobic segment and at least one hydrophilic segment.

5. Composition according to claim 4, characterized in that the hydrophobic segment is chosen from aliphatic chains, polyoxyalkylenes, alkylidene polyesters, polyethylene glycols with a benzyl polyether head, and cholesterol.

6. Composition according to claim 4 or 5, characterized in that the hydrophilic segment is chosen

from polyoxyalkylenes, polyvinyl alcohols, polyvinylpyrrolidones, or saccharides.

7. Composition according to one of the preceding claims, characterized in that the surface-active agent is a polyoxyalkylene of general formula:

$$HO(CH_2CH_2O)_a(CH(CH_3)CH_2O)_b(CH_2CH_2O)_cH$$

with a, b and c representing, independently of each other, integers which may vary between 20 and 100.

8. Composition according to one of the preceding claims, characterized in that it contains, as surface-active agent, a compound of general formula $OH(CH_2CH_2O)_a(CH(CH_3)CH_2O)_b(CH_2CH_2O)_cH$, with a equal to 75, b to 30 and c to 75.

9. Composition according to one of the preceding claims, characterized in that it contains, as surface-active agent, a compound of the family of polyethylene glycol with a dendritic benzyl polyether head.

10. Composition according to one of the preceding claims, characterized in that it contains, as surface-active agent, a compound of the polyoxyethylene alcohol family.

11. Composition according to one of the preceding claims, characterized in that it contains, as surface-active agent, polyoxyethylene nonylphenyl ether.

12. Composition according to one of the preceding claims, characterized in that the surface-

active agent is present therein at a concentration of between 0.01% and 10% weight/volume of the said composition.

13. Composition according to one of the preceding claims, characterized in that the surface-active agent is present therein at a concentration of between 0.02% and 5% weight/volume of the said composition.

14. Composition according to one of the preceding claims, characterized in that the cationic transfection agent is a lipofectant.

15. Composition according to claim 14, characterized in that the lipofectant is an amphiphilic molecule comprising at least one lipophilic region combined or otherwise with a hydrophilic region.

16. Composition according to claim 14, characterized in that it is a lipid mixture capable of forming cationic liposomes.

17. Composition according to claim 14 or 15, characterized in that it is a cationic lipid.

18. Composition according to claim 14 or 15, characterized in that it is a lipofectant comprising at least one polyamine region of general formula:

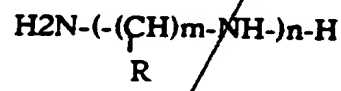
$$H_2N-(-(CH)_m-NH-)_n-H$$

in which m is an integer greater than or equal to 2 and n is an integer greater than or equal to 1, it being possible for m to vary between the different groups of carbon between 2 amines, this polyamine region being

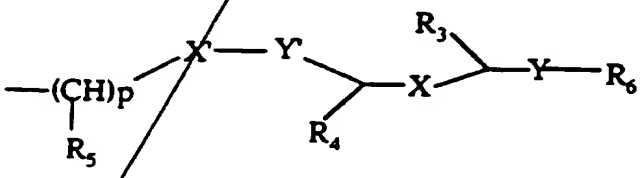
covalently combined with a lipophilic region of the saturated or unsaturated hydrocarbon chain of cholesterol type, or a natural or synthetic lipid capable of forming lamellar or hexagonal phases.

19. Composition according to claim 18, characterized in that the polyamine region is represented by spermine or one of its analogues which has conserved its nucleic acid-binding properties.

20. Composition according to claim 14 or 15, characterized in that it involves a lipofectant of general formula:



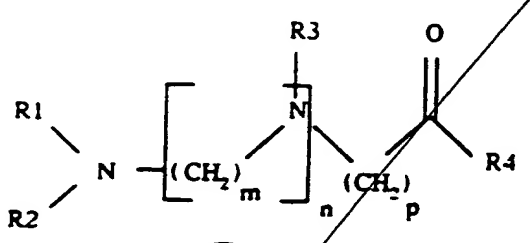
in which R denoting the lipophilic region is represented by the general formula:



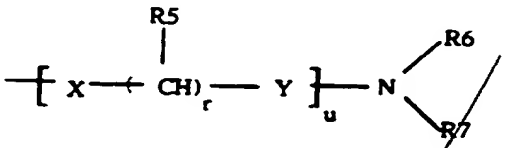
in which X and X' represent, independently of each other, an oxygen atom, a methylene group $-(CH_2)_q-$ with q equal to 0, 1, 2 or 3, or an amino group -NH- or -NR'-, with R' representing a C_1 to C_4 alkyl group, Y and Y' represent, independently of each other, a methylene group, a carbonyl group or a group C=S, R_3, R_4 and R_5 represent, independently of each other, a hydrogen atom or a substituted or unsubstituted C_1 to C_4 alkyl

radical, with p capable of varying between 0 and 5, R_6 represents a cholesterol derivative or an alkylamino group $-NR_1R_2$ with R_1 and R_2 representing, independently of each other, a saturated or unsaturated, linear or branched C_{12} to C_{22} aliphatic radical.

21. Composition according to claim 14 or 15, characterized in that it involves a lipofectant of general formula:



in which R_1, R_2 and R_3 represent, independently of each other, a hydrogen atom or a group $-(CH_2)_q-NRR'$ with q being capable of varying between 1, 2, 3, 4, 5 and 6, independently between the different groups R_1, R_2 and R_3 and R and R' representing, independently of each other, a hydrogen atom or a group $-(CH_2)_{q'}-NH_2$, q' being capable of varying between 1, 2, 3, 4, 5 and 6, independently between the different groups R and R', m, n and p represent, independently of each other, an integer capable of varying between 0 and 6 with, when n is greater than 1, m being capable of taking different values and R_3 different meanings within the preceding general formula and R_4 represents a group of general formula:



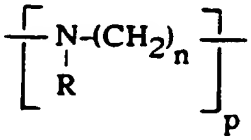
in which R_6 and R_7 represent, independently of each other, a hydrogen atom or a saturated or unsaturated C_{10} to C_{22} aliphatic radical with at least one of the two groups different from hydrogen, u is an integer chosen between 0 and 10 with, when u is an integer greater than 1, R_5, X, Y and r being capable of having different meanings within the different units $[X-(CHR_5)_r-Y]$, X represents an oxygen or sulphur atom, or an amine group which is monoalkylated or otherwise, Y represents a carbonyl group or a methylene group, R_5 represents a hydrogen atom or a natural amino acid side chain, substituted if appropriate, and r represents an integer varying between 1 and 10 with, when r is equal to 1, R_5 representing a substituted or unsubstituted natural amino acid side chain, and when r is greater than 1, R_5 representing a hydrogen atom.

22. Composition according to either of claims 14 and 15, characterized in that it involves a cationic lipid carrying one or more guanidinium and/or amidinium groups.

23. Composition according to one of claims 1 to 13, characterized in that the cationic transfection agent is a cationic polymer.

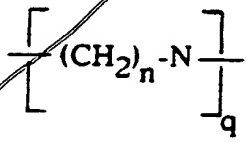
~~24. Composition according to claim 23,~~

characterized in that the said cationic polymer is a compound of general formula (I):



(I)

in which R may be a hydrogen atom or a group of formula:



n being an integer between 2 and 10, p and q being integers, it being understood that the sum p+q is such that the average molecular weight of the polymer is between 100 and 10^7 Da.

25. Composition according to claim 23 or 24, characterized in that it involves the polyethylene imine of average molecular weight 50,000 Da (PEI50K), the polyethylene imine of average molecular weight 22,000 Da (PEI22K) or the polyethylene imine of average molecular weight 800,000 Da (PEI800K).

26. Composition according to one of claims 1 to 14, characterized in that the cationic transfection agent is preferably chosen from lipofectamine, dioctadecylamidoglycyl spermine (DOGS), palmitoylphosphatidylethanolamine 5-carboxyspermylamide (DPPES), 2,5-bis(3-aminopropylamino)pentyl

(dioctadecylcarbamoylmethoxy)acetate or 1,3-bis(3-aminopropylamino)-2-propyl (dioctadecylcarbamoylmethoxy)acetate, $\{H_2N(CH_2)_3\}_2N(CH_2)_4N\{(CH_2)_3NH_2\}(CH_2)_3NHCH_2COGlyN[(CH_2)_{17}CH_3]_2$, $H_2N(CH_2)_3NH(CH_2)_4NH(CH_2)_3NHCH_2COGlyN[(CH_2)_{17}CH_3]_2$, and $H_2N(CH_2)_3NH(CH_2)_4NH(CH_2)_3NHCH_2COArgN[(CH_2)_{17}CH_3]_2$.

27. Composition according to one of the preceding claims, characterized in that the nucleic acid is a deoxyribonucleic acid.

28. Composition according to one of the preceding claims, characterized in that the nucleic acid is a ribonucleic acid.

29. Composition according to claim 27 or 28, characterized in that the nucleic acid is chemically modified.

30. Composition according to one of claims 1 to 26, characterized in that the nucleic acid is an antisense nucleic acid.

31. Composition according to one of the preceding claims, characterized in that the nucleic acid comprises a therapeutic gene.

32. Composition according to one of the preceding claims, characterized in that it comprises, in addition, an adjuvant of the type comprising dioleoylphosphatidylethanolamine (DOPE), oleoylpalmitoylphosphatidylethanolamine (POPE), di-stearoyl, -palmitoyl, -myristoyl phosphatidyl-ethanolamines as well as their derivatives which are

N-methylated 1 to 3 times, phosphatidylglycerols, diacylglycerols, glycosyldiacylglycerols, cerebrosides (such as in particular galactocerebrosides), sphingolipids (such as in particular sphingomyelins) or alternatively asialogangliosides.

33. Composition according to one of the preceding claims, characterized in that it combines, in addition, a targeting element with the cationic transfection agent.

34. Composition according to claim 33, characterized in that this targeting element is chosen from antibodies directed against molecules of the cellular surface, membrane receptor ligands such as insulin, transferrin, folic acid or any other growth factor, cytokines or vitamins, lectins, modified or otherwise, proteins with an RGD unit, peptides containing a tandem array of RGD units, cyclic or otherwise, polylysine peptides as well as natural or synthetic ligand peptides.

35. Process for the preparation of a composition comprising particles of cationic transfection agent(s)/nucleic acid complexes, characterized in that the transfecting agent and the nucleic acid are brought into contact in the presence of a sufficient quantity of a nonionic surface-active agent to stabilize the particles of nucleic complexes thus formed at a size of less than about 160 nm.

36. Process according to claim 35,

characterized in that one of the components chosen from the nucleic acid or the lipofectant is mixed beforehand with the nonionic surface-active agent before being brought into contact with the second component.

37. Process according to claim 35 or 36, characterized in that the surface-active agent is defined therein according to claims 4 to 13.